

What is claimed is:

1. A composition comprising a molecular complex formed between:

an alkaline pharmaceutical drug; and

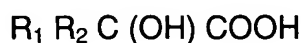
at least one agent selected from the group consisting of a hydroxyacid, a polyhydroxy acid, a related acid, a lactone form of these acids, and mixtures thereof.
2. The composition as claimed in claim 1, wherein the hydroxyacid is an alkyl alpha hydroxyacid represented by the formula:



wherein R_1 and R_2 may be independently H or alkyl group, and the alkyl alpha hydroxyacid may exist as stereoisomers as D, L and DL or R, S and RS forms when R_1 and R_2 are not identical.

3. The composition as claimed in claim 2, wherein the alkyl group is selected from one or more of the group consisting of methyl, ethyl, propyl, isopropyl, butyl, pentyl, octyl, lauryl, stearyl, and mixtures thereof.
4. The composition as claimed in claim 2, wherein the alkyl alpha hydroxyacid is selected from the group consisting of 2-hydroxyethanoic acid (glycolic acid), 2-hydroxypropanoic acid (lactic acid), 2-methyl-2-hydroxypropanoic acid (methyl lactic acid), 2-hydroxybutanoic acid, 2-hydroxypentanoic acid, 2-hydroxyhexanoic acid, 2-hydroxyheptanoic acid, 2-hydroxyoctanoic acid, 2-hydroxyeicosanoic acid (alpha hydroxyarachidonic acid), 2-hydroxytetraeicosanoic acid (cerebronic acid), 2-hydroxytetraeicosenoic acid (alpha hydroxynervonic acid), and mixtures thereof.

5. The composition as claimed in claim 1, wherein the hydroxyacid is an aralkyl hydroxyacid represented by the following formula:



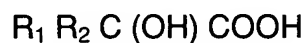
wherein R_1 and R_2 may be independently H, aryl, or aralkyl group, and the aralkyl hydroxyacid may exist as stereoisomers as D, L and DL or R, S and RS forms when R_1 and R_2 are not identical.

6. The composition as claimed in claim 5, wherein the aryl group is selected from the group consisting of phenyl, diphenyl, biphenyl, naphthyl, and mixtures thereof.

7. The composition as claimed in claim 5, wherein the aralkyl group is selected from the group consisting of phenylmethyl (benzyl), phenylethyl, phenylpropyl, diphenylmethyl, diphenylethyl, biphenylmethyl, naphthylmethyl group, and mixtures thereof.

8. The composition as claimed in claim 5, wherein the aralkyl hydroxyacid is selected from the group consisting of 2-phenyl-2-hydroxyethanoic acid (mandelic acid), 2,2-diphenyl-2-hydroxyethanoic acid (benzilic acid), 3-phenyl 2-hydroxypropanoic acid (3-phenyllactic acid), 2-phenyl-2-methyl-2-hydroxyethanoic acid (atrolactic acid, 2-phenyllactic acid), and mixtures thereof.

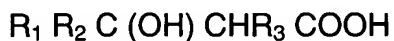
9. The composition as claimed in claim 1, wherein the hydroxyacid is a polycarboxy alpha hydroxyacid represented by the following formula:



where R_1 and R_2 may be independently H, COOH, CH_2COOH or CHOHCOOH , and the polycarboxy AHAs may exist as stereoisomers as D, L and DL or R, S and RS forms when R_1 and R_2 are not identical.

10. The composition as claimed in claim 9, wherein the polycarboxy alpha hydroxyacid is selected from the group consisting of 2-hydroxypropane-1,3-dioic acid (tartronic acid), 2-hydroxybutane-1,4-dioic acid (malic acid), 2,3-dihydroxybutane-1,4-dioic acid (tartaric acid), 2-hydroxy-2-carboxypentane-1,5-dioic acid (citric acid), isocitric acid, and mixtures thereof.

11. The composition as claimed in claim 1, wherein the hydroxyacid is a beta hydroxyacid represented by the following formula:



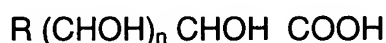
where R_1 , R_2 , R_3 may be H, alkyl, aryl or aralkyl group, and where the beta hydroxyacid may exist as stereoisomers as D, L and DL or R, S and RS forms when R_1 and R_2 are not identical or R_3 is not H.

12. The composition as claimed in claim 11, wherein the beta hydroxyacid is selected from the group consisting of 3-hydroxypropanoic acid (β -hydroxypropanoic acid), 3-hydroxybutanoic acid (β -hydroxybutanoic acid), 3-hydroxypentanoic acid, 3-hydroxy-2-phenylpropanoic acid (tropic acid), and mixtures and combinations thereof.

13. The composition as claimed in claim 1, wherein the hydroxyacid is a polyhydroxy acid.

14. The composition as claimed in claim 13, wherein the polyhydroxy acid is selected from the group consisting of aldonic acids, aldaric acids, alduronic acids, and mixtures thereof.

15. The composition as claimed in claim 14, wherein the aldonic acid is represented by the following formula.

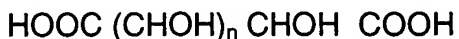


where R is H or alkyl group, and n is an integer from 1-6, and where the aldonic acids may exist as stereoisomers as D, L and DL, or R, S and RS forms.

16. The composition as claimed in claim 15, wherein the aldonic acid is selected from the group consisting of 2,3-dihydroxypropanoic acid (glyceric acid), 2,3,4-trihydroxybutanoic acids (stereoisomers; erythronic acid and erythrulose, threonic acid and threulose), 2,3,4,5-tetrahydroxypentanoic acids (stereoisomers; ribonic acid and ribulose, arabinoic acid and arabinulose, xylonic acid and xylulose, lyxonic acid and lyxulose), 2,3,4,5,6-pentahydroxyhexanoic acids (stereoisomers; allonic acid and allulose, altronic acid and altrulose, gluconic acid and gluconolactone, mannoic acid and mannulose, gulonic acid and gulonolactone, idonic acid and idonolactone, galactonic acid and galactonolactone, talonic acid and talonolactone), 2,3,4,5,6,7-hexahydroxyheptanoic acids (stereoisomers; alloheptonic acid and alloheptonolactone, altroheptonic acid and altroheptonolactone, glucoheptonic acid and glucoheptonolactone, mannoheptonic acid and mannoheptonolactone, guloheptonic acid and guloheptonolactone, idoheptonic

acid and idoheptonolactone, galactoheptonic acid and galactoheptonolactone, taloheptonic acid and taloheptonolactone), and mixtures thereof.

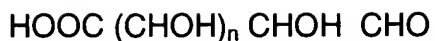
17. The composition as claimed in claim 14, wherein the aldaric acid is represented by the following formula:



where n is an integer from 1-4, and where the aldaric acids may exist as stereoisomers as D, L and DL, or R, S and RS forms.

18. The composition as claimed in claim 17, wherein the aldaric acids is selected from the group consisting of 2,3-dihydroxybutane-1,4-dioic acids (stereoisomers; erythraric acid and threarric acid, also known as tartaric acid), 2,3,4-trihydroxypentane-1,5-dioic acids (stereoisomers; ribaric acid and ribarolactone, arabaric acid and arabarolactone, xylaric acid and xylarolactone, lyxaric acid and lyxarolactone), 2,3,4,5-tetrahydroxyhexane-1,6-dioic acids (stereoisomers; allaric acid and allarolactone, altraric acid and altrarolactone, glucaric acid and glucarolactone, mannaric acid and mannarolactone, gularic acid and gularolactone, idaric acid and idarolactone, galactaric acid and galactarolactone, talaric acid and talarolactone), 2,3,4,5,6-pentahydroxyheptane-1,7-dioic acids (stereoisomers; alloheptaric acid and alloheptarolactone, altoheptaric acid and altoheptarolactone, glucoheptaric acid and glucoheptarolactone, mannoheptaric acid and mannoheptarolactone, guloheptaric acid and guloheptarolactone, idoheptaric acid and idoheptarolactone, galactoheptaric acid and galactoheptarolactone, taloheptaric acid and taloheptarolactone), and mixtures thereof.

19. The composition as claimed in claim 14, wherein the alduronic acid is represented by the following formula:



where n is an integer from 1-4, and where the alduronic acids may exist as stereoisomers as D, L and DL, or R, S and RS forms.

20. The composition as claimed in claim 19, wherein the alduronic acid is selected from the group consisting of erythruronic acid, threuronic acid, riburonic acid and riburonolactone, arabinuronic acid and arabinuronolactone, xyluronic acid and xyluronolactone, lyxuronic acid and lyxuronolactone, alluronic acid and alluronolactone, altruronic acid and altruronolactone, glucuronic acid and glucuronolactone, mannuronic acid and mannuronolactone, guluronic acid and guluronolactone, iduronic acid and iduronolactone, galacturonic acid and galacturonolactone, taluronic acid and taluronolactone, allohepturonic acid and allohepturonolactone, altohepturonic acid and altohepturonolactone, glucohepturonic acid and glucohepturonolactone, mannohepturonic acid and mannohepturonolactone, gulohepturonic acid and gulohepturonolactone, idohepturonic acid and idohepturonolactone, galactohepturonic acid and galactohepturonolactone, talohepturonic acid and talohepturonolactone, and mixtures thereof.

21. The composition as claimed in claim 1, wherein the hydroxyacid is an aldobionic acid represented by the following generic formula:



where m and n are integers independently from 0-7, and R is a monosaccharide, and wherein the aldobionic acid exists as stereoisomers as D, L and DL, or R, S and RS forms, and can form intramolecular lactones by the removal of one mole of water between the carboxyl group and one hydroxyl group.

22. The composition as claimed in claim 1, wherein the hydroxyacid is an aldobionic acid selected from the group consisting of lactobionic acid and lactobionolactone, isolactobionic acid and isolactobionolactone, maltobionic acid and maltobionolactone, isomaltobionic acid and isomaltobionolactone, cellobionic acid and cellobionolactone, gentiobionic acid and gentiobionolactone, kojibionic acid and kojibionolactone, laminaribionic acid and laminaribionolactone, melibionic acid and melibionolactone, nigerobionic acid and nigerobionolactone, rutinobionic acid and rutinobionolactone, sophorobionic acid and sophorobionolactone, and mixtures thereof.

23. The composition as claimed in claim 1, wherein the related acids are selected from the group consisting of alpha ketoacids, miscellaneous hydroxyacids, oligomers of hydroxyacids, and mixtures thereof.

24. The composition as claimed in claim 23, wherein the alpha ketoacid is represented by the following formula:

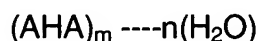


wherein Ra is H, alkyl, aralkyl or aryl group of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 25 carbon atoms, and in addition Ra may carry F, Cl, Br, I, OH, CHO, COOH and alkoxy group having 1 to 9 carbon atoms.

25. The composition as claimed in claim 24, wherein the alpha ketoacid is selected from the group consisting of: 2-ketoethanoic acid (glyoxylic acid), 2-ketopropanoic acid (pyruvic acid), 2-phenyl-2-ketoethanoic acid (benzoylformic acid), 3-phenyl-2-ketopropanoic acid (phenylpyruvic acid), 2-ketobutanoic acid, 2-ketopentanoic acid, 2-ketohexanoic acid, 2-ketoheptanoic acid, 2-ketooctanoic acid, 2-ketododecanoic acid, and mixtures thereof.

26. The composition as claimed in claim 23, wherein the miscellaneous hydroxyacid is selected from the group consisting of: agaricic acid, aleuritic acid, citramalic acid, glucosaminic acid, galactosaminic acid, 2-keto-gulonic acid and 2-keto-gulonolactone, mannosaminic acid, mevalonic acid and mevalonolactone, pantoic acid and pantolactone, quinic acid (1,3,4,5-tetrahydroxycyclohexanecarboxylic acid), piscidic acid (4-hydroxybenzyltartaric acid), ascorbic acid (3-oxo-L-gulofuranolactone), Isoascorbic acid (D-erythro-hex-2-enonic acidr-lactone), 2-hexulosonic acids (isomers; arabino-2-hexulosonicacid, xylo-2-hexulosonic acid, ribo-2-hexulosonic acid, lyxo-2-hexulosonic acid), 5-hexulosonic acids (isomers; arabino-5-hexulosonic acid, xylo-5-hexulosonic acid, ribo-5-hexulosonic acid, lyxo-5-hexulosonic acid), and mixtures thereof.

27. The composition as claimed in claim 23, wherein the oligomer of hydroxyacid is represented by the following general formula:



wherein, AHA is a hydroxyacid, $m=2-10$, with a preferred number of 2-4, and $n=m-1$, and wherein the AHA in each monomer needs not be identical.

28. The composition as claimed in claim 27, wherein the oligomer of hydroxyacid is selected from the group consisting of glycolyl glycolate, lactyl lactate, citryl citrate, glycoly citrate, citryl glycolate, lactyl citrate, citryl lactate, maly malate, maly glycolate, tartaryl tartrate, tartaryl glycolate, glycolyl tartrate, glycolyl glycoly glycolate, lactyl lactyl lactate, and mixtures thereof.

29. The composition as claimed in claim 1, wherein the hydroxacid, polyhydroxy acid, related acid, or lactone of these acids is selected from one or more of the group consisting of glycolic acid, lactic acid, gluconic acid, gluconolactone, ribonic acid, ribonolactone, galactonic acid, galactonolactone,

glucoheptonic acid, glucoheptonolactone, glucuronic acid, glucuronolactone, galacturonic acid, galacturonolactone, glucaric acid, glucarolactone, galactaric acid, galactarolactone, lactobionic acid, maltobionic acid, and mixtures thereof.

30. The composition as claimed in claim 1, wherein the alkaline pharmaceutical drug is selected from the group consisting of acebutolol, acetohydroxamic acid, actiq, acyclovir, albuterol, allopurinol, alloxanthine, alprazolam, alprenolol, amiloride, amantadine, aminacrine, amitriptyline, amorolfine, amodiaquin, amocarzine, amoxapine, atenolol, bemegride, benzocaine, bepridil, benztropine, bupivacaine, bupropion, burimamide, brompheniramine, butoconazole, caffeine, carbamazepine, chlordiazepoxide, chloroquine, chlorpheniramine, chlorpromazine, cimetidine, clonidine, cocaine, codeine, cyclizine, chlorhexidine, citalopram, clemastine, clindamycin, clioquinol, clotrimazole, clozapine, cromolyn, crotamiton, cyclizine, cycloserine, dexmedetomidine, dicyclomine, dihydromorphine, diphenhydramine, diphenoxylate, disopyramide, dobutamine, dopamine, dopamide, dopa esters, doxepin, doxylamine, dyclonine, desipramine, diazepam, dihydrocodeine, diphenoxylate, ephedrine, epinephrine, epinine, ergotamine, econazole, erythromycin, etidocaine, etomidate, fentanyl, fluoxetine, fluphenazine, flurazepam, fluvoxamine, guanethidine, guaifenesin, N-guanylhistamine, haloprogin, hydralazine, hypoxanthine, ichthammol, imiquimod, indomethacin, imipramine, irbesartan, isoetharine, isoproterenol, ketamine, ketanserin, ketoconazole, ketoprofen, kanamycin, labetalol, lamotrigine, lidocaine, lobeline, losartan, loxapine, lysergic diethylamide, mafenide, maprotiline, mecamlamine, meclizine, meclocycline, meperidine, mepivacaine, mescaline, metanephrine, metaproterenol, methadone, methoxamine, metiamide, metolazone, metronidazole, miconazole, midazolam, minocycline, minoxidil, mirtazapine, mupirocin metaraminol, methadone, methamphetamine, methyl dopamide, methyl dopa esters, metoprolol, mexiletine, molindone,

morphine, moxonidine, 3,4-methylenedioxymethamphetamine, nadolol, naftifine, naloxone, nefazodone, neomycin, nifedipine, nystatin, nicotine, norepinephrine, octopamine, olanzapine, ondansetron, oxiconazole, oxotremorine, oxymetazoline, paroxetine, pentazocine, phencyclidine, pheniramine, phenmetrazine, phentolamine, phenylephrine, phenylpropanolamine, phenelzine, phenoxybenzamine, physostigmine, pilocarpine, pimozide, pipamazine, pirenzepine, podophyllin, podofilox, pramipexole, pramoxine, prenalterol, prilocaine, procaine, promethazine propionate, propranolol, protriptyline, pseudoephedrine, pyrethrin, pyrilamine, pentazocine, phenylephrine, physostigmine, pilocarpine, pindolol, prazosin, procainamide, procaine, promazine, promethazine, propranolol, pseudoephedrine, pyrimethamine, quetiapine, quinethazone, quinidine, reserpine, risperidone, ritodrine, ropinirole, ropivacaine, salmeterol, scopolamine, selegiline, serotonin, sertindole, sertraline, sotalol, strychnine, sulconazole, sulfadiazine, sulfanilamide, tamsulosin, tazarotene, terbinafine, terconazole, terfenadine, tetracaine, tetracycline, tetrahydrozoline, theobromine, theophylline, thymol, timolol, tioconazole, tizanidine, tocainide, tolnaftate, tranylcypromine, trazodone, triamterene, triazolam, triflupromazine, tripelennamine, triprolidine, terbutaline, thioridazine, tyramine, tolazoline, xanthine, venlafaxine, verapamil and ziprasidone, and mixtures thereof.

31. The composition as claimed in claim 1, wherein the molar ratio of the alkaline pharmaceutical drug to the hydroxyacid or polyhydroxy acid or related acid or lactone is within the range of from about 1:0.1 to about 1:40.

32. The composition as claimed in claim 1, wherein the molar ratio of the alkaline pharmaceutical drug to the hydroxyacid or polyhydroxy acid or related acid or lactone is within the range of from about 1:0.5 to about 1:5.

33. The composition as claimed in claim 1, wherein the molecular weight of the hydroxyacid, or polyhydroxyacid, or related acid, or lactone form thereof is within the range of from about 50 to about 1000.

34. The composition as claimed in claim 1, wherein the molecular weight of the hydroxyacid, or polyhydroxyacid, or related acid, or lactone form thereof is within the range of from about 70 to about 700.

35. The composition as claimed in claim 1, further comprising pharmaceutical and other topical agents selected from the group consisting of: those that improve or eradicate age spots, keratoses and wrinkles; local analgesics and anesthetics; antiacne agents; antibacterials; antiyeast agents; antifungal agents; antiviral agents; antidandruff agents; antidermatitis agents; antihistamine agents; antipruritic agents; antiemetics; antimotionsickness agents; antiinflammatory agents; antihyperkeratolytic agents; antiperspirants; antipsoriatic agents; antiseborrheic agents; hair conditioners and hair treatment agents; antiaging and antiwrinkle agents; sunblock and sunscreen agents; skin lightening agents; depigmenting agents; vitamins; corticosteroids; tanning agents; humectants; hormones; retinoids; gum disease or oral care agents; topical cardiovascular agents; corn, callus and wart removing agents; dipilating agents, and mixtures and combinations thereof.

36. The composition as claimed in claim 1, further comprising one or more additional agents selected from the group consisting of aclovate, acetylsalicylic acid, adapalene, aluminum acetate, aluminum chloride, aluminum hydroxide, aluminum chlorohydroxide, aminobenzoic acid (PABA), aminocaproic acid, aminosaliclic acid, anthralin, ascorbic acid, ascoryl palimate, azelaic acid, bacitracin, beclomethasone dipropionate, benzophenone, benzoyl peroxide, betamethasone dipropionate, betamethasone valerate, calcipotriene, camphor, capsaicin, carbamide peroxide, chitosan, chloroxylonol, ciclopirox, clobetasol

propionate, coal tar, dehydroepiandrosterone, desoximetasone, dexamethasone, estradiol, ethinyl estradiol, fluocinonide, fluocinolone acetonide, 5-fluorouracil, griseofulvin, hexylresorcinol, homosalate, hydrocortisone, hydrocortisone 21-acetate, hydrocortisone 17-valerate, hydrocortisone 17-butyrate, hydrogen peroxide, hydroquinone, hydroquinone monoether, hydroxyzine, ibuprofen, indomethacin, kojic acid, menthol, methyl nicotinate, methyl salicylate, monobenzone, naproxen, octyl methoxycinnamate, octyl salicylate, oxybenzone, padimate O, permethrin, phenol, piperonyl butoxide, povidone iodine, resorcinol, retinal, 13-cis retinoic acid, retinoic acid, retinol, retinyl acetate, retinyl palmitate, salicylamide, salicylic acid, selenium sulfide, shale tar, sulfur, triamcinolone diacetate, triamcinolone acetonide, triamcinolone hexacetonide, triclosan, undecylenic acid, urea, vitamin E acetate, wood tar, zinc pyrithione, N-acetyl-prolinamide, N-acetyl-lysine, N-acetyl-ornithine, N-acetyl-glucosamine, and mixtures thereof.

37. A method of forming a molecular complex between an alkaline pharmaceutical drug and at least one of a hydroxyacid, polyhydroxyacid, related acid, and lactone, comprising:

dissolving the alkaline pharmaceutical drug and an alkali in a suitable reaction medium to form a free base of the pharmaceutical drug;

optionally separating the free base of the pharmaceutical drug from the reaction medium; and

adding at least one of a hydroxyacid, a polyhydroxyacid, a related acid, or lactones thereof to the free base in a suitable reaction medium to form a molecular complex.

38. The method as claimed in claim 37, wherein the free base of the pharmaceutical drug is separated from the reaction medium.

39. The method as claimed in claim 37, wherein the reaction medium used to form the free base of the pharmaceutical drug is water.
40. The method as claimed in claim 37, wherein the alkali added to the alkaline pharmaceutical drug is an inorganic alkali.
41. The method as claimed in claim 37, wherein the free base of the alkaline pharmaceutical drug is formed as a precipitate or oily product that then is separated from the reaction medium.
42. The method as claimed in claim 37, wherein the reaction medium used to form the molecular complex is water, and wherein the free base of the alkaline pharmaceutical drug is suspended in the water.
43. The method as claimed in claim 42, wherein the reaction medium additionally comprises a solvent selected from the group consisting of ethanol, propylene glycol, butylene glycol, and mixtures thereof.
44. The method as claimed in claim 37, wherein the molecular complex is formed when the pH of the reaction medium has changed.
45. The method as claimed in claim 37, wherein the amount of hydroxyacid, polyhydroxy acid, related acid, or lactone form thereof is within the range of from about 0.1 to about 40 moles per mole of pharmaceutical drug.
46. The method as claimed in claim 45, wherein the amount of hydroxyacid, polyhydroxy acid, related acid, or lactone form thereof is within the range of from about 0.5 to about 5 moles per mole of pharmaceutical drug.
47. A method of treating a cosmetic condition or dermatologic indication in a subject comprising topically administering a therapeutically effective amount of the composition as claimed in claim 1 to a subject in need thereof.

48. The method as claimed in claim 47, wherein the pH of the composition is within the range of from about 2.0 to about 7.0

49. The method as claimed in claim 48, wherein the pH of the composition is within the range of from about 3.0 to about 5.0.

50. The method as claimed in claim 47, wherein the composition is in a form selected from the group consisting of lotion, cream, ointment, and gel.

51. The method as claimed in claim 50, wherein the composition additionally includes a cosmetically or dermatologically acceptable excipient.

52. The method as claimed in claim 47, wherein the method treats, heals or prevents a cosmetic condition or dermatological indication.

53. The method as claimed in claim 52, wherein the method treats, heals, or prevents a cosmetic condition or dermatological indication selected from the group consisting cosmetic and clinical signs of changes associated with intrinsic or extrinsic aging; the damages caused by extrinsic factors such as sunlight, air pollution, wind, cold, dampness, heat, chemicals, smoke, cigarette smoking, and radiations including electromagnetic radiations and ionizing radiations; mucosa; skin erythema; inflammation or reaction caused by internal or external factors; and mixtures thereof.

54. The method as claimed in claim 52, wherein the cosmetic condition or dermatological indication is selected from the group consisting of: disturbed keratinization; inflammation; defective syntheses of dermal components; changes associated with intrinsic and extrinsic aging of skin, nail and hair; dryness or looseness of skin, nail and hair; xerosis; ichthyosis; palmar and plantar hyperkeratoses; uneven and rough surface of skin, nail and hair; dandruff; Darier's disease; lichen simplex chronicus; keratoses; acne;

pseudofolliculitis barbae; dermatoses; eczema; psoriasis; pruritus; warts; herpes; age spots; lentigines; melasmas; blemished skin; hyperkeratoses; hyperpigmented or hypopigmented skin; abnormal or diminished syntheses of collagen, glycosaminoglycans, proteoglycans and elastin as well as diminished levels of such components in the dermis; stretch marks; skin lines; fine lines; wrinkles; thinning of skin, nail plate and hair; skin thickening due to elastosis of photoaging, loss or reduction of skin, nail and hair resiliency, elasticity and recoilability; lack of skin, nail and hair lubricants and luster; dull and older-looking skin, nail and hair; fragility and splitting of nail and hair, or used as to lighten the skin.

55. The method as claimed in claim 54, wherein the skin changes associated with aging are selected from the group consisting of progressive thinning of skin, fragile skin, deepening of skin lines and fine lines, wrinkles including fine and coarse wrinkles, lusterless skin surface, coarse and uneven skin, loss of skin elasticity and recoilability, blemished and leathery skin, loss of skin lubricating substances, increased numbers of blotches and mottles, nodules, pre-cancerous lesions, pigmented spots and mottled skin, changes in qualities and quantities of collagen and elastic fibers, solar elastosis, decrease in collagen fibers, diminution in the number and diameter of elastic fibers in the papillary dermis, atrophy of the dermis, stretch marks, reduction in subcutaneous adipose tissue and deposition of abnormal elastic materials in the upper dermis, yellowing skin, telangiectatic skin, and older-looking skin.